UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,768	09/24/2003	Yuqiao Shen	ONYX1047-DIV	8135

37499 7590 08/14/2008

ONYX PHARMACEUITICALS, INC.
2100 POWELL STREET
12TH FLOOR
EMERYVILLE, CA 94608

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/669,768	SHEN ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 July 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *15 July 2008*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *13,25-27 and 35-38*.
   Claim(s) rejected: *11,12,24,28,33,39 and 40*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Maria B Marvich, PhD/
Primary Examiner, Art Unit 1633

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments filed 7/15/08 have been fully considered but they are not persuasive.Applicants argue that the specification teaches one how to create recombinant adenovirus of the present invention as well as methods of identifying recombinant adenoviruses having the desired characteristics. As well, applicants argue that the dependent claims that are not subjected to the rejection under 35 USC 112, first paragraph mirror the independent claims. As to this later issue, the independent claims are drawn to a "recombinant adenovirus comprising a mutation in the E1B-55K gene". In contrast, the virus of for example claim 13 which is "Onyx 051" is a rAd with a single mutation and therefore the virus has a mutated sequence wherein the sequence "consists" of a single amino acid substitution. By the open language, the instantly recited rAd "comprises" the single amino acid substitution and hence can comprise any number of insertions, deletions and substitutions. Both claim 11 and 33 are rejected for this language.

Hence, applicants claims are drawn to a large genus of recombinant adenovirus (rAd) which only need require a single amino acid substitution in the E1B 55K gene. Multiple further modifications are encompassed by the claims. The mutation however, must function to reduce the ability of the recombinant adenovirus to bind p53. Predicting the functional nature of any of these rAd is an unpredictable art as set forth in the rejection. Applicants have only demonstrated the operability of the claimed invention for two single amino acid substitutions in the E1B 55K gene as set forth in Onyx 051 and Onyx 053. No other rAd comprising nucleic acid with single amino acid substitutions generated provided the desired function other then these two viruses. As to the operability of other mutations, applicants own results demonstrate the unpredictability of identifying mutants with a particular function. However, the instant claims are drawn to a genus of rAd that encompass single amino acid substitutions but also comprise any number of insertions, deletions, substitutions or any other modifications. Yet, the specification does not provide any guidance as to those regions that can tolerate such modifications and yet provide an intact rAd that can mediate treatment of cancer in the presence of chemotherapy such that binding ofp53 is reduced. Applicants only demonstrate that they have provided adequate guidance to support the two examples. It is noted that though not controlling, the lack of working examples, is, nevertheless, a factor to be considered in a case involving both physiological activity and an undeveloped art. When a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the examiner may, properly, ask for evidence to substantiate them. Ex parte Sudilovsky, 21 USPQ2d 1702, 1705 (BPAI 1991); In re Novak, 134 USPA 335 (CCPA 1962); In re Fouche, 169 USPQ 429 (CCPA 1971).

As stated in Capon "The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science." Capon also states "It is well recognized that in the "unpredictable" fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the exemplification in the specification". Hence, the broad nature of the claims coupled with the lack of guidance in the specification and the demonstration in the art of the unpredictability of varied effects of rAd function, the methods are highly unpredictable and this unpredictability is evidenced by applicants own results. Kirn et al does nothing to demonstrate that the genus of recited viruses can be identified other then extending the species of viruses that have lost ability to bind p53 to inclusion of Onyx 015. However, Onyx 015 does not consist of a single amino acid substitution and hence does not meet the requirements that E1B55K has a single amino acid substitution. Rather Onyx 015 is attenuated by deletion of a large part of the coding sequence for E1B 55K. Even should applicants limit the claims to consisting of this single amino acid substitution, there are still 26 mutants that by not functioning indicate that the question is not undue experimentation as it appears that no amount of experimentation will identify other single amino acid substitutions that have reduced p53 binding and treat cancer in combination with chemotherapy.

The MPEP teaches that the "As to the patentability of the instant case in light of similar claims in published patents that possess similar disclosures, rejections based upon this argument have been addressed in in re Giolito and Hoffman. "It is immaterial whether similar claims have been allowed to others" (see in re Giolito and Hoffman 188 USPQ 645). Rather, each application is reviewed on its own merits." In this case, applicants have not described additional single amino acid mutations. However, more importantly the claims have been accessed in light of the disclosure in combination with the prior art as to whether the specification enables one skilled in the art to make and use the genus of adenovirus. The lack of enablement of the instant claims rests with two factors. First, when considering the species of recited rAd that are single amino acid mutants, applicants own results demonstrate that the ability to identify rAd single amino acid mutations that have reduced p53 binding such that they can be used with chemotherapy to treat cancer is highly unpredictable. Hence, additional members of this group do not appear to exist. Secondly, a large genus of rAd are claim by recitation that the rAd comprises the single amino acid mutation and applicants have not provided any guidance as to other modifications that would be used in connection with the single amino acid substitutions. One could not begin to guess amongst the incredible board and diverse genus of additional modifications as to which are desired. It is quite simply unpredictable that amongst this genus those viruses with desired functions could be identified.

As to the patentability of the instant case in light of similar claims in published patents that possess similar disclosures, rejections based upon this argument have been addressed in in re Giolito and Hoffman. "It is immaterial whether similar claims have been allowed to others" (see in re Giolito and Hoffman 188 USPQ 645). Rather, each application is reviewed on its own merits.